

**RECEIVED****REGISTERED****PATENT COOPERATION TREATY**

APR 20 2006

**MUETING & RAASCH**

From the INTERNATIONAL SEARCHING AUTHORITY

**PCT**

SLA

To:  
**MUETING, RAASCH & GEBHARDT, P.A.**  
 Attn. Sandberg, Victoria A.  
 P.O. Box 581415  
 Minneapolis, Minnesota 55458-1415  
 UNITED STATES OF AMERICA

**INVITATION TO PAY ADDITIONAL FEES**

(PCT Article 17(3)(a) and Rule 40.1)

4/28/06 Romandie  
 5/7/06 Resp DSB

		Date of mailing (day/month/year)	07/04/2006
Applicant's or agent's file reference 235.00550201 ✓	<b>PAYMENT DUE</b>	within ONE MONTH from the above date of mailing	
International application No. PCT/US2004/037896 ✓	International filing date (day/month/year)	12/11/2004	
Applicant <b>THE UNIVERSITY OF GEORGIA RESEARCH FOUNDATION INC.</b>			

## 1. This International Searching Authority

- (i) considers that there are 3 (number of) inventions claimed in the international application covered by the claims indicated ~~XXXX~~on the extra sheet:

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated ~~XXXX~~on the extra sheet:

- (ii)  has carried out a partial international search (see Annex)  will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:  
 see annex

- (iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid

## 2. The applicant is hereby invited, within the time limit indicated above, to pay the amount indicated below:

EUR 1.615,00 x 2 = EUR 3.230  
 Fee per additional invention      number of additional inventions      total amount of additional fees

Or, \_\_\_\_\_ x \_\_\_\_\_ = \_\_\_\_\_

The applicant is informed that, according to Rule 40.2(c), the payment of any additional fee may be made under protest, i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3.  Claim(s) Nos. \_\_\_\_\_ have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer <b>Sylvia Hermier</b>
---	---

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-4, and part of 6-35

A method of introducing a compound into a Gram negative bacterial cell as claimed.  
---

2. claims: 5, and part of 6-35

Method for identifying a compound having antimicrobial activity according to these claims.  
---

3. claims: 36-42

An antimicrobial compound, a pharmaceutical composition containing it, a method of treatment in which it is used, and its first or second medical use as defined in these claims.  
---

In the present application, three problems are identified. For each of these problems, a different solution is proposed.

The first problem defined in the claims is the provision of a method for introducing a peptide or a peptidomimetic into a Gram negative bacterial cell. As a solution to this problem, biotinylation is proposed (claims 1-3 and their depending claims).

The second problem defined in the claims is the provision of a method of identifying a compound having antimicrobial activity. As a solution, the Gram negative bacterial cell is contacted with a biotinylated derivative of the compound (claim 5 and its depending claims).

The third problem to be solved is the provision of an antimicrobial compound, a pharmaceutical composition containing it, a method of treatment in which it is used, and its first or second medical use. The solution to this problem is, however, not well defined. In fact, any compound having antimicrobial activity falls under the definition used in claims 36-42.

The technical feature linking a priori inventions 1 and 2 as identified above is the biotinylation of a compound, with the penetration of the resulting conjugate into Gram negative bacterial cells.

The technical feature linking a priori inventions 2 and 3 as identified above is a compound having antimicrobial effects.

Both technical features are, however, already known from DARGIS M ET AL: "Use of biotinylated beta-lactams and chemiluminescence for study and purification of penicillin-binding proteins in bacteria." ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, vol. 38, no. 5, May 1994 (1994-05), pages 973-980, ISSN: 0066-4804.

which describes the antibiotic effect of biotinylated ampicilline in the Gram negative bacterium H. influenzae. As the skilled person knows, ampicilline itself also has an antimicrobial effect.

In view of this document, neither of the technical features linking a priori the different subjects contained in the present application can serve as special technical feature in the sense of Rule 13 PCT, linking these subjects together. Since there is no other technical feature, that could fulfil the role of special technical feature in the sense of Rule 13 PCT, the present application lacks unity of invention, containing the subject-matters as listed.

Although some document cited in the present search report may also be pertinent for further inventions mentioned this does not imply, that the search for those subjects has been fully performed.

As searching the other inventions and establishing the Written Opinion of the International Search Authority (WO-ISA) requires more than only "negligible additional work", the search and Written Opinion have been restricted to the first invention only, see also the PCT International Search and Preliminary Examination Guidelines, 10.65.

The applicant is warned that the third invention may prove to be unsearchable, due to the lack of definition of the compound as defined by the wording of these claims.

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:
 

see 'Invitation to pay additional fees'
2. This communication is not the international search report which will be established according to Article 18 and Rule 43.
3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.
4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DARGIS M ET AL: "Use of biotinylated beta-lactams and chemiluminescence for study and purification of penicillin-binding proteins in bacteria." ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, vol. 38, no. 5, May 1994 (1994-05), pages 973-980, XP002374249 ISSN: 0066-4804 abstract page 975, right-hand column, last paragraph	1-4,6-35
X	WO 99/06440 A (ACADEMISCH ZIEKENHUIS BIJ DE UNIVERSITEIT VAN AMSTERDAM; APPELMELK, BE) 11 February 1999 (1999-02-11) page 15, line 22 - page 17, line 5	1-4,6-35
X	DE 100 55 789 A1 (PHARMA-ZENTRALE GMBH) 6 June 2002 (2002-06-06) examples	1-4,6-35

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RAMANATHAN S ET AL: "Targeted PEG-based bioconjugates enhance the cellular uptake and transport of a HIV-1 TAT nonapeptide" JOURNAL OF CONTROLLED RELEASE, ELSEVIER, AMSTERDAM, NL, vol. 77, no. 3, 13 December 2001 (2001-12-13), pages 199-212, XP004328573 ISSN: 0168-3659 cited in the application page 200, right-hand column, last paragraph - page 201, right-hand column	1-4,6-35
X	WO 98/52614 A (THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY; ROTHBA) 26 November 1998 (1998-11-26) examples 8,11	1-4,6-35
X	WO 90/12096 A (PURDUE RESEARCH FOUNDATION) 18 October 1990 (1990-10-18) example 12	1-4,6-35
X	LING LING CHEN ET AL: "INCREASED CELLULAR UPTAKE OF THE HUMAN IMMUNODEFICIENCY VIRUS-1 TATPROTEIN AFTER MODIFICATION WITH BIOTIN" ANALYTICAL BIOCHEMISTRY, ACADEMIC PRESS, SAN DIEGO, CA, US, vol. 227, 1995, pages 168-175, XP002927982 ISSN: 0003-2697 page 168, right-hand column page 169, right-hand column figures 2,3,5	1-4,6-35
Y	EP 1 036 798 A (HISAMITSU PHARMACEUTICAL CO. INC; HISAMITSU PHARMACEUTICAL CO., INC) 20 September 2000 (2000-09-20) example 1	1-4,6-35
Y	WO 95/31556 A (UNILEVER NV; UNILEVER PLC) 23 November 1995 (1995-11-23) example 1	1-4,6-35
Y	STOLZ ET AL: "rapid purification of a functionally active sucrose carrier from transgenic yeast using a bacterial biotin acceptor domain" FEBS LETTERS, ELSEVIER, AMSTERDAM, NL, no. 377, 1995, pages 167-171, XP002079374 ISSN: 0014-5793 page 167 - page 168	1-4,6-35
Y	US 5 976 535 A (FRITZBERG ET AL) 2 November 1999 (1999-11-02) the whole document	1-4,6-35

Annex Form PCT/ISA/206  
**COMMUNICATI RELATING TO THE RESULTS  
 OF THE PARTIAL INTERNATIONAL SEARCH**

ational Application No  
**PCT/US2004/037896**

**C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>OTVOS LASZLO JR ET AL: "Interaction between heat shock proteins and antimicrobial peptides"          BIOCHEMISTRY,          vol. 39, no. 46,          21 November 2000 (2000-11-21), pages          14150-14159, XP002374250          ISSN: 0006-2960          abstract          page 14151, right-hand column - page          14152, left-hand column          -----</p>	1-4,6-35
E	<p>WO 2005/032598 A (THE GENERAL HOSPITAL CORPORATION; ELMALEH, DAVID, R; SHOUP, TIMOTHY, M) 14 April 2005 (2005-04-14)          page 2, last paragraph - page 3, line 10          page 42, line 30 - page 43, line 7          page 44, line 23 - line 32          -----</p>	1-4,6-35

**Patent Family Annex**

Information on patent family members

National Application No

PCT/US2004/037896

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9906440	A	11-02-1999	AU	759636 B2	17-04-2003
			AU	3787097 A	22-02-1999
			CA	2298101 A1	11-02-1999
			EP	0988314 A1	29-03-2000
			JP	2001512140 T	21-08-2001
			US	6624140 B1	23-09-2003
DE 10055789	A1	06-06-2002	AU	3722002 A	27-05-2002
			WO	0240511 A2	23-05-2002
WO 9852614	A	26-11-1998	AT	251913 T	15-11-2003
			AU	734827 B2	21-06-2001
			AU	7593898 A	11-12-1998
			BR	9809138 A	28-08-2001
			CA	2291074 A1	26-11-1998
			CN	1263473 A	16-08-2000
			DE	69818987 D1	20-11-2003
			DE	69818987 T2	29-07-2004
			EP	0975370 A2	02-02-2000
			ES	2210761 T3	01-07-2004
			GB	2341390 A	15-03-2000
			JP	2002502376 T	22-01-2002
			PL	337033 A1	31-07-2000
WO 9012096	A	18-10-1990	AT	160583 T	15-12-1997
			AU	5437590 A	05-11-1990
			CA	2013580 A1	03-10-1990
			CA	2013582 A1	03-10-1990
			DE	69031763 D1	08-01-1998
			DE	69031763 T2	25-06-1998
			DK	466816 T3	10-08-1998
			EP	0466816 A1	22-01-1992
			ES	2113346 T3	01-05-1998
			IE	901201 A1	09-10-1991
			IL	93983 A	18-02-1997
			JP	5502787 T	20-05-1993
			JP	3232347 B2	26-11-2001
			PT	93646 A	20-11-1990
			US	5108921 A	28-04-1992
			US	5416016 A	16-05-1995
EP 1036798	A	20-09-2000	AT	245168 T	15-08-2003
			DE	60003860 D1	21-08-2003
			DE	60003860 T2	05-02-2004
			JP	2000264900 A	26-09-2000
			US	6451971 B1	17-09-2002
WO 9531556	A	23-11-1995	EP	0759081 A1	26-02-1997
			JP	10500127 T	06-01-1998
US 5976535	A	02-11-1999	NONE		
WO 2005032598	A	14-04-2005	NONE		